Merck Research Laboratories
HER2 and CEA Plasmid Vaccine

The non-technical abstract

The targets of this vaccine trial are the tumor antigens HER2 and carcinoembryonic antigen (CEA). HER2 is an oncogene that encodes a growth factor receptor that is involved in the unregulated growth of adenocarcinomas. The HER2 gene becomes amplified during cancer growth and, as a consequence, the HER2 protein is overexpressed in tumor cells. The unregulated expression of this protein alters the growth control processes of the cell rendering it malignant. CEA is also overexpressed in adenocarcinoma cells. Its function is probably tightly connected with the capacity of the tumor to spread and metastasize to distant locations. Thus, these two antigens have been selected as targets for the immune response because driving the immune system to selectively act against these two proteins will probably direct it specifically against the tumor cells since these cells overexpress the two antigens. Additionally, targeting the immune response to proteins that play important roles in tumor development may also lead to an enhanced antitumor effect since the immune response will perturb the functionality of elements needed by the tumor for its growth and expansion. Furthermore, although the tumor cell is genetically unstable and changes its expression profile as it grows and expands, it is highly unlikely that CEA and HER2 will be simultaneously lost during tumor growth in view of their biological function needed for tumor progression.

The vaccine V930 is based on the use of plasmid DNA that encode CEA and HER2 modified to enhance immunogenicity and antitumor effects. The vaccine V930 will be administered in conjunction with an electrical impulse using a technique called electroporation (EP). DNA-EP has been shown to increase the efficacy of plasmid DNA vaccines in preclinical models leading to an enhanced antigen expression and increased immune response. The mechanism for this enhancement is due, in part, to an increased uptake of plasmid DNA by the muscle cells, which become transiently permeabilized upon electrical stimulation, allowing the DNA to enter into the cell and more specifically into the nucleus, with greater efficiency. The increased uptake of plasmid by the muscle cells allows for greater expression of the target antigen leading to a stronger immune response and, ultimately, to a better antitumor effect.

Plasmid DNA vaccines are easy to make and can express a number of different tumor antigens; therefore a vaccination targeting multiple antigenic components of the tumor cell is possible. Targeting multiple antigens through this approach will undoubtedly enhance the therapeutic impact of vaccination on tumor growth.

The aims of this trial are to: (a) determine the safety of a plasmid DNA vaccine administered in conjunction with EP to cancer patients whose tumors express CEA and/or HER2; (b) determine the immunogenicity of DNA-EP vaccine for CEA and HER2; and (c) Assess whether the dose of the CEA and HER2 plasmids impacts the development of an immune response to these target antigens.